08/459,141

Logon file405 10oct95 10:10:59
ANNOUNCEMENT **** ANNOUNCEMENT **** ANNOUNCEMENT

***New: Business & Industry (File 9)
Newspaper Abstracts Daily(TM) (File 483)

***Reload: Environmental Bibliography (File 68)
IAC Business A.R.T.S. (File 88)
(formerly Academic Index)
Books in Print (File 470)
Periodical Abstracts PlusText (File 484)
(formerly Newspaper & Periodical Abstracts)

Don't forget to register for Knight-Ridder Information's UPDATE '95!
...See September Chronolog for details

Win $500! Sept search contest entries performed in a market research file due by October 11, 1995

Free connect time and output in Business & Industry (File 9); Free October 1
Alerts in Business & Industry (File 9) and IAC Industry Express (File 12)...See HELP FREE for details

Message from database supplier:
MEDLINE and CANCERLIT erroneously annotated certain articles authored or co-authored by Dr. Bernard Fisher with the phrase "scientific misconduct--data to be reanalyzed." All such annotations have been removed or are being removed. We apologize for any problems or concerns this may have caused. Users should disregard those prior annotations.

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<
>>> Announcements last updated for 2oct95 <<<
F130: Due To Update Problems, Today's Data Is Not Yet Available, Pls Try Again Later .
SYSTEM:HOME
Menu System II: D2 version 1.7.3 term=ASCII
*** DIALOG HOMEBASE(SM) Main Menu ***

Information:
1. Announcements (new files, free connect time, price changes, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:
6. DIALOG Menus(SM)
7. DIALOG Business Connection(R), Headlines(SM), Medical Connection(SM)
8. DIALOG SourceOne(SM) Document Delivery
9. Data-Star
10. Other Online Menu Services & Files (MoneyCenter(R), OAG, TNT, etc.)

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online

service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
?begin biochem

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       10oct95 10:11:22 User214374 Session B131.1
            $0.00    0.006 Hrs FileHomeBase
     $0.00  Estimated cost FileHomeBase
     $0.07  SPRNTNET
     $0.07  Estimated cost this search
     $0.07  Estimated total session cost   0.006 Hrs.

SYSTEM:OS  - DIALOG OneSearch
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         (c) 1995 BIOSIS
*File   5: s (Meeting()Abstract) or abstracts/DE for 1994+ conference
records
  File  73:EMBASE  1974-1995/Iss 39
         (c) 1995 Elsevier Science B.V.
  File  76:Life Sciences Collection  1978-1995/Aug
         (c) 1995 Cambridge Sci Abs
  File 125:CLAIMS(R)/US PATENT  JUL 1995/OCT 03
         (c) 1995 IFI/Plenum Data Corp
  File 144:Pascal  1973-1995/Sep
         (c) 1995 INIST/CNRS
  File 155:MEDLINE(R)  1966-1995/Nov W4
         (c) format only 1995 Knight-Ridder Info
  File 156:Toxline(R)  1965-1995/May
         (c) format only 1995 Knight-Ridder Info
  File 305:Analytical Abstracts Online  1980-1995/Oct
         (c) 1995 Royal Soc Chemistry
  File 337:CHEMTOX(R)   1995/Q2
         (c) 1995 Resource Consultants, Inc.
  File 340:CLAIMS(R)/US Patents Abs  1950-1995/JUL
         (c) 1995 IFI/Plenum Data Corp.
  File 348:EUROPEAN PATENTS  1978-1995/SEP W4
         (c) 1995 European Patent Office
*File 348: Fulltext is forthcoming.  See HELP NEWS 348 for
more information.
  File 350:Derwent World Pat.  1963-1980/UD=9536
         (c) 1995 Derwent Info Ltd
  File 351:DERWENT WPI  1981-1995/UD=9539;UA=9533;UM=9528
         (c)1995 Derwent Info Ltd
  File 357:Derwent Biotechnology Abs  1982-1995/Oct B1
         (c) 1995 Derwent Publ Ltd
  File 358:Current Biotech Abs  1983-1995/Aug
         (c) 1995 Royal Society of Chemistry
*File 358: May 1995 update is in process and should complete later
today (09 Jun 1995).  Subsequent updates should be back on schedule.
  File 377:Derwent Drug File  1983-1995/Oct W1
         (c) 1995 Derwent Info Ltd.
  File 399:CA SEARCH(R)  1967-1995/UD=12315
         (c) 1995 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
  File 434:SciSearch(R)  1974-1995/Sep W3
         (c) 1995 Inst for Sci Info
  File 442:AMA Online Journal  1982-1995/Aug W4
         (c) 1995 American Medical Assoc.
*File 442: AMA Journals Online updates weekly beginning with UD=9504W3.
  File 444:NEJM Online  1985-1995/Sep W3
         (c) 1995 New England Journal of Medicine.
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  File 456:NME Express  1992-1995/Aug B2
         (c) 1995 J.R. Prous S.A.
*File 456: Bi-Weekly ALERTs now available.
  File 624:McGraw-Hill Publications Onl.  1985-1995/Oct 05
         (c) 1995 McGraw-Hill
*File 624: Please type 'E JN=' for all current journals available.

      Set  Items  Description
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?s herpes(4w)simplex(4w)virus
Processing
Processed  10 of  22 files ...
Completed processing all files
          153332  HERPES
          132020  SIMPLEX
         1534248  VIRUS
      S1   92464  HERPES(4W)SIMPLEX(4W)VIRUS
?
PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
?
TIMEOUT: Logged Off 10/10/95 10:24:44 by System

DIALOG DISCONNECTED 00 40 00:00:14:28 145 9

@c dialog


DIALOG CONNECTED

DIALOG INFORMATION SERVICES
PLEASE LOGON:
?##########
ENTER PASSWORD:
?##########
Welcome to DIALOG

Dialog level 38.09.06B

Reconnected in file BIOCHEM 10oct95 10:26:12

SYSTEM:OS  - DIALOG OneSearch
  File   5:BIOSIS PREVIEWS(R)  1969-1995/Oct W2
         (c) 1995 BIOSIS
*File   5: s (Meeting()Abstract) or abstracts/DE for 1994+ conference
records
  File  73:EMBASE  1974-1995/Iss 39
         (c) 1995 Elsevier Science B.V.
  File  76:Life Sciences Collection  1978-1995/Aug
         (c) 1995 Cambridge Sci Abs
  File 125:CLAIMS(R)/US PATENT  JUL 1995/OCT 03
         (c) 1995 IFI/Plenum Data Corp
  File 144:Pascal  1973-1995/Sep
         (c) 1995 INIST/CNRS
  File 155:MEDLINE(R)  1966-1995/Nov W4
         (c) format only 1995 Knight-Ridder Info
  File 156:Toxline(R)  1965-1995/May
         (c) format only 1995 Knight-Ridder Info
  File 305:Analytical Abstracts Online  1980-1995/Oct
         (c) 1995 Royal Soc Chemistry
  File 337:CHEMTOX(R)   1995/Q2
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        (c) 1995 Resource Consultants, Inc.
  File 340:CLAIMS(R)/US Patents Abs  1950-1995/JUL
        (c) 1995 IFI/Plenum Data Corp.
  File 348:EUROPEAN PATENTS  1978-1995/SEP W4
        (c) 1995 European Patent Office
*File 348: Fulltext is forthcoming.  See HELP NEWS 348 for
more information.
  File 350:Derwent World Pat.  1963-1980/UD=9536
        (c) 1995 Derwent Info Ltd
  File 351:DERWENT WPI  1981-1995/UD=9539;UA=9533;UM=9528
        (c)1995 Derwent Info Ltd
  File 357:Derwent Biotechnology Abs  1982-1995/Oct B1
        (c) 1995 Derwent Publ Ltd
  File 358:Current Biotech Abs  1983-1995/Aug
        (c) 1995 Royal Society of Chemistry
*File 358: May 1995 update is in process and should complete later
today (09 Jun 1995).  Subsequent updates should be back on schedule.
  File 377:Derwent Drug File  1983-1995/Oct W1
        (c) 1995 Derwent Info Ltd.
  File 399:CA SEARCH(R)  1967-1995/UD=12315
        (c) 1995 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
  File 434:SciSearch(R)  1974-1995/Sep W3
        (c) 1995 Inst for Sci Info
  File 442:AMA Online Journal  1982-1995/Aug W4
        (c) 1995 American Medical Assoc.
*File 442: AMA Journals Online updates weekly beginning with UD=9504W3.
  File 444:NEJM Online  1985-1995/Sep W3
        (c) 1995 New England Journal of Medicine.
  File 456:NME Express  1992-1995/Aug B2
        (c) 1995 J.R. Prous S.A.
*File 456: Bi-Weekly ALERTs now available.
  File 624:McGraw-Hill Publications Onl.  1985-1995/Oct 05
        (c) 1995 McGraw-Hill
*File 624: Please type 'E JN=' for all current journals available.

      Set  Items  Description
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?s herpes(4w)simplex(4w)virus
Processing
Processed  10 of  22 files ...
Completed processing all files
         153332  HERPES
         132020  SIMPLEX
        1534248  VIRUS
      S2   92464  HERPES(4W)SIMPLEX(4W)VIRUS
?s vaccine and s2
         236655  VACCINE
          92464  S2
      S3    3212  VACCINE AND S2
?s polypeptide
      S4  252753  POLYPEPTIDE
?s membrane(4w)bound
Processing
Processed  10 of  22 files ...
Completed processing all files
        1906526  MEMBRANE
         556448  BOUND
      S5   68983  MEMBRANE(4W)BOUND
?s s3 and s4
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            3212  S3
          252753  S4
      S6     100  S3 AND S4
?s s6 and s5
             100  S6
           68983  S5
      S7      10  S6 AND S5
?rd
>>>Duplicate detection is not supported for File 125.
>>>Duplicate detection is not supported for File 337.
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 350.
>>>Duplicate detection is not supported for File 351.
>>>Duplicate detection is not supported for File 456.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S8       7  RD (unique items)
?t s8/6/1-7

 8/6/1     (Item 1 from file: 5)
11478401     BIOSIS Number: 98078401
  Expression and characterization of baculovirus expressed herpes simplex
virus type 1 glycoprotein L
  Print Number: Biological Abstracts Vol. 099 Iss. 004 Ref. 048811


 8/6/2     (Item 1 from file: 155)
09344285   95274285
  Expression  of  membrane-bound and secreted forms of equine herpesvirus 1
glycoprotein D by recombinant baculovirus.


 8/6/3     (Item 1 from file: 351)
004272169  WPI Acc No: 85-099047/17
XRAM Acc No: C85-042865
    Vaccine contg. poly. peptide with exposed antigenic determinants useful
    for giving protection against herpes simplex virus


 8/6/4     (Item 1 from file: 357)
036148  DBA Accession No.: 85-06937
Membrane-bound polypeptide having antigenic determinants - useful for
    binding to herpes simplex virus


 8/6/5     (Item 2 from file: 357)
036147  DBA Accession No.: 85-06936
Vaccine containing polypeptide with exposed antigenic determinants - useful
    for giving protection against herpes simplex virus


 8/6/6     (Item 1 from file: 434)
13663171   Genuine Article#: QF404   Number of References: 27
Title: EXPRESSION OF MEMBRANE-BOUND AND SECRETED FORMS OF EQUINE
    HERPESVIRUS-1 GLYCOPROTEIN-D BY RECOMBINANT BACULOVIRUS  (Abstract
    Available)
```

8/6/7 (Item 1 from file: 444)
00102344

Patterns of Persistent Viral Infections (Medical Progress)
?t s8/6/1-7

8/6/1 (Item 1 from file: 5)
11478401 BIOSIS Number: 98078401
Expression and characterization of baculovirus expressed herpes simplex virus type 1 glycoprotein L
Print Number: Biological Abstracts Vol. 099 Iss. 004 Ref. 048811

8/6/2 (Item 1 from file: 155)
09344285 95274285
Expression of membrane-bound and secreted forms of equine herpesvirus 1 glycoprotein D by recombinant baculovirus.

8/6/3 (Item 1 from file: 351)
004272169 WPI Acc No: 85-099047/17
XRAM Acc No: C85-042865
Vaccine contg. poly. peptide with exposed antigenic determinants useful for giving protection against herpes simplex virus

8/6/4 (Item 1 from file: 357)
036148 DBA Accession No.: 85-06937
Membrane-bound polypeptide having antigenic determinants - useful for binding to herpes simplex virus

8/6/5 (Item 2 from file: 357)
036147 DBA Accession No.: 85-06936
Vaccine containing polypeptide with exposed antigenic determinants - useful for giving protection against herpes simplex virus

8/6/6 (Item 1 from file: 434)
13663171 Genuine Article#: QF404 Number of References: 27
Title: EXPRESSION OF MEMBRANE-BOUND AND SECRETED FORMS OF EQUINE HERPESVIRUS-1 GLYCOPROTEIN-D BY RECOMBINANT BACULOVIRUS (Abstract Available)

8/6/7 (Item 1 from file: 444)
00102344

Patterns of Persistent Viral Infections (Medical Progress)
?t s8/5/1-7

8/5/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11478401 BIOSIS Number: 98078401
Expression and characterization of baculovirus expressed herpes simplex virus type 1 glycoprotein L
Ghiasi H; Kaiwar R; Slanina S; Nesburn A B; Wechsler S L
Ophthalmol. Res., Davis Bldg. Rm 5072, Cedars-Sinai Med. Cent., 8700

Beverly Blvd., Los Angeles, CA 90048, USA
Archives of Virology 138 (3-4). 1994. 199-212.
Full Journal Title: Archives of Virology
ISSN: 0304-8608
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 004 Ref. 048811

We have constructed a recombinant baculovirus expressing high levels of the herpes simplex virus type 1 (HSV-1) glycoprotein L (gL) in Sf9 cells. Sf9 cells infected with this recombinant virus synthesized three polypeptides of 26-27 kDa 28 kDa, and 31 kDa. The 28 and 31 kDa species were sensitive to tunicamycin and N-glycosidase F (PNGase F) treatment, suggesting that they were glycosylated. As shown by both indirect immunofluorescence and Western blot analysis, using polyclonal antibodies to synthetic gL peptides indicated that the baculovirus expressed gL was abundant on the surface of baculovirus gL infected Sf9 cells. A small fraction of the 31 kDa polypeptide was secreted into the extracellular medium as judged by Western blot analysis. The secreted form of gL was completely resistant to Endoglycosidase H (Endo-H), while the membrane associated form of gL was only partially resistant to Endo-H treatment, suggesting that the secreted gL represented a subpopulation of the membrane bound gL. Mice vaccinated with baculovirus expressed gL produced serum antibodies that reacted with authentic HSV-1 gL. However, these mice produced no HSV-1 neutralizing antibody (titer lt 1: 10) and they were not protected from lethal intraperitoneal or lethal ocular challenge with HSV-1. Thus, when used as a vaccine in the mouse model, gL, similar to our findings with HSV-1 gH, but unlike our results with the other 6 HSV-1 glycoproteins that we have expressed in this baculovirus system, did not provide any protection against HSV-1 challenge.

Descriptors/Keywords: RESEARCH ARTICLE; MOUSE; SF9 CELLS; GLYCOSYLATION; SURFACE EXPRESSION; SECRETION; VACCINE SUITABILITY; CHALLENGE PROTECTION; GENETIC ENGINEERING

Concept Codes:
*10064 Biochemical Studies-Proteins, Peptides and Amino Acids
*10068 Biochemical Studies-Carbohydrates
*10508 Biophysics-Membrane Phenomena
*13004 Metabolism-Carbohydrates
*13012 Metabolism-Proteins, Peptides and Amino Acids
*22018 Pharmacology-Immunological Processes and Allergy
*31500 Genetics of Bacteria and Viruses
*33506 Virology-Animal Host Viruses
*34504 Immunology and Immunochemistry-Bacterial, Viral and Fungal
*36006 Medical and Clinical Microbiology-Virology
*64076 Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology

Biosystematic Codes:
02603 Baculoviridae (1993-)
02612 Herpesviridae (1993-)
75330 Lepidoptera
86375 Muridae

Super Taxa:
Microorganisms; Viruses; Animals; Invertebrates; Arthropods; Insects; Chordates; Vertebrates; Nonhuman Vertebrates; Mammals; Nonhuman Mammals ; Rodents

8/5/2 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09344285 95274285

Expression of membrane-bound and secreted forms of equine herpesvirus 1 glycoprotein D by recombinant baculovirus.

Flowers CC; Flowers SP; Sheng Y; Tarbet EB; Jennings SR; O'Callaghan DJ
Department of Microbiology and Immunology, Louisiana State University Medical Center, Shreveport 71130-3932, USA.

Virus Res (NETHERLANDS) Jan 1995, 35 (1) p17-34, ISSN 0168-1702
Journal Code: X98
Contract/Grant No.: AI 22001, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9508
Subfile: INDEX MEDICUS

Analyses of the synthesis and processing of recombinant full-length glycoprotein D of equine herpesvirus type 1 (EHV-1; gD392) or recombinant truncated gD (gD352) expressed in baculovirus-infected Sf9 cells revealed the following: (1) gD polypeptides encoded by both recombinant baculoviruses react with gD-specific antibodies including peptide-specific antiserum that neutralizes EHV-1 in a plaque reduction assay, (2) both the full-length recombinant gD392 and the truncated gD352 are expressed predominantly as gD species that contain high mannose-type oligosaccharides (55 kDa and 52 kDa, respectively), (3) both the full-length recombinant gD392 and the truncated gD352 are also expressed in lesser amounts as gD species that contain complex-type oligosaccharides (58 kDa and 55 kDa, respectively) as well as the unglycosylated forms of gD (43 kDa and 37 kDa, respectively), (4) flow cytometric analyses of cells expressing gD392 revealed that gD first appears on the cell surface at 24 h post infection; by 60 h, 95% of the cells express high levels of cell surface gD, (5) cells expressing gD352, in contrast to cells expressing gD392, secrete gD into the extracellular medium. This initial demonstration that immunoreactive EHV-1 glycoprotein D can be produced as a secreted polypeptide in the baculovirus system should provide reagents to assess the potential use of gD as a subunit vaccine in an animal model.

Tags: Animal; Comparative Study; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: *Genetic Vectors--Genetics--GE; *Herpesvirus 1, Equid --Genetics--GE; *Membrane Proteins--Biosynthesis--BI; *Nuclear Polyhedrosis Virus--Genetics--GE; *Recombinant Fusion Proteins--Biosynthesis--BI; *Viral Envelope Proteins--Biosynthesis--BI; Antibodies, Viral--Immunology--IM; Cell Line; Glycosylation; Herpesvirus 1, Equid--Immunology--IM; Membrane Proteins--Genetics--GE; Membrane Proteins--Immunology--IM; Oligosaccharide s--Analysis--AN; Protein Processing, Post-Translational; Recombinant Fusion Proteins--Immunology--IM; Recombinant Fusion Proteins--Secretion--SE; Spodoptera; Viral Envelope Proteins--Genetics--GE; Viral Envelope Proteins --Immunology--IM; Viral Envelope Proteins--Secretion--SE
CAS Registry No.: 0 (glycoprotein D, herpes simplex virus type 1); 0 (Antibodies, Viral); 0 (Genetic Vectors); 0 (Membrane Proteins); 0 (Oligosaccharides); 0 (Recombinant Fusion Proteins); 0 (Viral Envelope Proteins)

8/5/3 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

004272169 WPI Acc No: 85-099047/17
XRAM Acc No: C85-042865
Vaccine contg. poly. peptide with exposed antigenic determinants useful for giving protection against herpes simplex virus
Patent Assignee: (GETH) GENENTECH INC
Author (Inventor): LASKY L A; BERMAN P W

Number of Patents: 010
Patent Family:

CC	Number	Kind	Date	Week	
AU	8432423	A	850307	8517	(Basic)
EP	139417	A	850502	8518	
ZA	8406764	A	850228	8523	
DK	8404122	A	850411	8536	
JP	60155128	A	850815	8539	
ES	8605039	A	860801	8644	
ES	8705036	A	870701	8730	
EP	139417	B	890726	8930	
DE	3479085	G	890831	8936	
IL	72785	A	900726	9035	

Priority Data (CC No Date): US 588170 (840309); US 527917 (830830); US 547551 (831031)
Applications (CC,No,Date): AU 8432423 (840827); EP 84305909 (840829); ZA 846764 (840829); JP 84183623 (840830); ES 535554 (840830); ES 552539 (860228)
Language: English
EP and/or WO Cited Patents: EP 73656; EP 68693; EP 101655; WO 8302897; US 4374127; US 4317811; EP 1365; DE 2949031; 3.Jnl.REF; EP 60129; EP 100521; EP 133063
Designated States (Regional): AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
Filing Details: EP0139417 (+31.10.83-US-547551) (1248AP); JP60155128 (+31.10.83-US551)5 (44pp); EP0139417 (+31.10.83-US-547551) (CM)

Abstract (Basic): AU 8432423

Vaccine comprising a membrane-bound polypeptide (I) having exposed antigenic determinants capable of raising neutralising antibodies against a pathogen is new. The (I) is functionally associated with a membrane of a recombinant, stable, continuous cell line capable of its prodn.

The vaccine may also comprise a membrane-free (I), dissolved free from the membrane after its prodn. is new.

Vaccine comprising a truncated membrane-free deriv. of a membrane-bound (I) is new. The deriv. is devoid of membrane-binding domain and the deriv. (I) is free from the membrane and has exposed antigenic determinants capable of raising neutralising antibodies against a pathogen.

USE/ADVANTAGE - Membrane bound (I) and membrane free (I) are useful as vaccines to give protection against herpes simplex viruses 3 and/or 2 by raising antibodies against them. Therefore the occurrence of herpes infections or redn. in frequency and severity in individuals already infected can be achieved. See AU8432424. @(93pp Dwg.No 0/16)@

Abstract (EP): 8930 EP 139417

A process which comprises producing a truncated, membrane-free deviation of a membrane-bound polypeptide, said derivative being devoid of membrane-binding domain whereby the derivative polypeptide is free of said membrane, and having exposed antigenic determinants capable of raising neutralising antibodies against a pathogen, said method comprising expressing DNA encoding said derivative in a stable eukaryotic cell line transfected with said DNA. @(53pp)@

File Segment: CPI
Derwent Class: B04; D16;
Int Pat Class: A61K-039/00; C07C-103/52; C07H-021/04; C12N-015/00; C12N-005/00; C12P-021/00; C12R-001/91; C07K-015/16
Manual Codes (CPI/A-N): B02-V; B04-B02B; B04-B04C; B04-C01; B12-A06; D05-H07
Chemical Fragment Codes (M1):
01 M421 M710 M903 N135 P210 Q233 V274 V901

8/5/4 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

036148 DBA Accession No.: 85-06937 PATENT
Membrane-bound polypeptide having antigenic determinants - useful for binding to herpes simplex virus
PATENT ASSIGNEE: Genentech 1985
PATENT NUMBER: AU 8432424 PATENT DATE: 850307 WPI ACCESSION NO.: 85-099048 (8517)
PRIORITY APPLIC. NO.: US 587763 APPLIC. DATE: 840309
NATIONAL APPLIC. NO.: AU 8432424 APPLIC. DATE: 840827
LANGUAGE: English
ABSTRACT: A diagnostic product comprising membrane-bound polypeptide (I) having antigenic determinants capable of specific binding of complementary antibody is new. The (I) is functionally associated with a membrane of a recombinant stable continuous cell line capable of its production. A diagnostic kit is also described. Membrane-bound (I) are useful as diagnostic agents and are obtained in large amounts by recombinant DNA technology in non-pathogenic form. They may be obtained from a stable continuous cell line. As (I) are especially capable of binding herpes simplex virus specific antibodies, they may also be used in vaccines against the virus or to reduce the effects of an existing infection. The (I) is especially a glycoprotein (C or D) of herpes simplex virus type 1 or 2 and is capable of binding to the antibodies. It may be a fragment of glycoprotein C and then binds to types 1 or 2 or to type 1 alone. It may be linked to a label e.g. an enzyme, or to a solid surface. The diagnostic kit may contain unlabeled and labeled complementary antibody. (95pp)
DESCRIPTORS: cloned membrane-bound polypeptide prep., appl. to diagnosis, vaccine prep. for e.g. herpes simplex virus
SECTION: Pharmaceuticals-Vaccines; Cell Culture-Animal Cell Culture; Microbiology-Genetics (D4,J1,A1)

8/5/5 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

036147 DBA Accession No.: 85-06936 PATENT
Vaccine containing polypeptide with exposed antigenic determinants - useful for giving protection against herpes simplex virus
PATENT ASSIGNEE: Genentech 1985
PATENT NUMBER: AU 8432423 PATENT DATE: 850307 WPI ACCESSION NO.: 85-099047 (8517)
PRIORITY APPLIC. NO.: US 588170 APPLIC. DATE: 840309
NATIONAL APPLIC. NO.: AU 8432423 APPLIC. DATE: 840827
LANGUAGE: English
ABSTRACT: A vaccine comprising a membrane-bound polypeptide (I) having exposed antigenic determinants capable of raising neutralizing antibodies against a pathogen is new. The (I) is functionally associated with a membrane of a recombinant stable, continuous cell line capable of its production. The vaccine may comprise a membrane-free (I) dissolved free from the membrane after its production. A vaccine comprising a truncated membrane-free derivative of a membrane-bound (I) is also described. The derivative is devoid of membrane-binding domain and the derivative (I) is free from the membrane and has exposed antigenic determinants capable of raising

neutralizing antibodies against a pathogen. Membrane-bound (I) and membrane-free (I) are useful as vaccines to give protection against herpes simplex virus 1 and/or 2. The recombinant host cell is a stable eukaryotic cell line or a mammalian cell line, and (I) is especially a glycoprotein of herpes simplex virus type 1 or 2. (93pp)
DESCRIPTORS: membrane-bound polypeptide vaccine prep. for e.g. herpes simplex virus, cell culture
SECTION: Pharmaceuticals-Vaccines; Cell Culture-Animal Cell Culture (D4,J1)

8/5/6 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R)

13663171 Genuine Article#: QF404 Number of References: 27
Title: EXPRESSION OF MEMBRANE-BOUND AND SECRETED FORMS OF EQUINE HERPESVIRUS-1 GLYCOPROTEIN-D BY RECOMBINANT BACULOVIRUS
Author(s): FLOWERS CC; FLOWERS SP; SHENG YW; TARBET EB; JENNINGS SR; OCALLAGHAN DJ
Corporate Source: LOUISIANA STATE UNIV,MED CTR,DEPT MICROBIOL & IMMUNOL,1501 KINGS HIGHWAY/SHREVEPORT//LA/71130; LOUISIANA STATE UNIV,MED CTR,DEPT MICROBIOL & IMMUNOL/SHREVEPORT//LA/71130
Journal: VIRUS RESEARCH, 1995, V35, N1 (JAN), P17-34
ISSN: 0168-1702
Language: ENGLISH Document Type: ARTICLE
Geographic Location: USA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: VIROLOGY
Abstract: Analyses of the synthesis and processing of recombinant full-length glycoprotein D of equine herpesvirus type 1 (EHV-1; gD392) or recombinant truncated go (gD352) expressed in baculovirus-infected Sf9 cells revealed the following: (1) go polypeptides encoded by both recombinant baculoviruses react with go-specific antibodies including peptide-specific antiserum that neutralizes EHV-1 in a plaque reduction assay, (2) both the full-length recombinant gD392 and the truncated gD352 are expressed predominantly as go species that contain high mannose-type oligosaccharides (55 kDa and 52 kDa, respectively), (3) both the full-length recombinant gD392 and the truncated gD352 are also expressed in lesser amounts as go species that contain complex-type oligosaccharides (58 kDa and 55 kDa, respectively) as well as the unglycosylated forms of go (43 kDa and 37 kDa, respectively), (4) flow cytometric analyses of cells expressing gD392 revealed that go first appears on the cell surface at 24 h post infection; by 60 h, 95% of the cells express high levels of cell surface go, (5) cells expressing gD352, in contrast to cells expressing gD392, secrete go into the extracellular medium. This initial demonstration that immunoreactive EHV-1 glycoprotein D can be produced as a secreted polypeptide in the baculovirus system should provide reagents to assess the potential use of go as a subunit vaccine in an animal model.
Descriptors--Author Keywords: EQUINE HERPESVIRUS TYPE 1 ; GLYCOPROTEIN D ; BACULOVIRUS ; SECRETED GD
Identifiers--KeyWords Plus: SIMPLEX VIRUS TYPE-1; UNIQUE SHORT SEGMENT; D GENE; SEQUENCE-ANALYSIS; HOMOLOG; IDENTIFICATION; VECTORS; GENOME
Research Fronts: 93-2767 002 (BACULOVIRUS EXPRESSION SYSTEM; INSECT CELLS; AUTOGRAPHA-CALIFORNICA NUCLEAR POLYHEDROSIS-VIRUS; RECOMBINANT VIRAL INSECTICIDES)
93-0591 001 (HERPES-SIMPLEX VIRUS TYPE-1; TRANSPORT CAPSID ASSEMBLY PROTEIN (TP CAP) GENE; EXHIBIT ALTERED VIRAL THYMIDINE KINASE EXPRESSION)

Cited References:
ALLEN GP, 1987, V61, P2454, J VIROL
AUDONNET JC, 1990, V71, P2969, J GEN VIROL
COHEN GH, 1984, V49, P102, J VIROL
DENHURK SVL, 1991, V65, P263, J VIROL
EISENBERG RJ, 1982, V56, P1014, J VIROL
ELDER JH, 1982, V79, P4540, P NATL ACAD SCI USA
ELTON DM, 1992, V73, P1227, J GEN VIROL
FLOWERS CC, 1992, V66, P6451, J VIROL
FLOWERS CC, 1991, V180, P175, VIROLOGY
FLOWERS CC, 1992, V190, P307, VIROLOGY
GHIASI H, 1991, V121, P163, ARCH VIROL
GHIASI H, 1994, V68, P2118, J VIROL
KRISHNA S, 1989, V70, P1805, J GEN VIROL
LANDOLFI V, 1993, V11, P407, VACCINE
LASKY LA, 1984, V2, P527, BIO-TECHNOL
LOVE DN, 1993, V67, P6820, J VIROL
LOVE DN, 1992, V30, P387, VET MICROBIOL
LUCKOW VA, 1988, V6, P47, BIOTECHNOLOGY
MILLER LK, 1988, V42, P177, ANNU REV MICROBIOL
MUGGERIDGE MI, 1990, V2, P459, IMMUNOCHEMISTRY VIRU
OCALLAGHAN DJ, 1968, V36, P104, VIROLOGY
SISK WP, 1994, V68, P766, J VIROL
SUMMERS MD, 1987, MANUAL METHODS BACUL
TELFORD EAR, 1992, V189, P304, VIROLOGY
THOMSEN DR, 1990, V43, P67, J CELL BIOCHEM
WHALLEY M, 1991, V5, P313, VIRUS GENES
WHITTAKER GR, 1992, V73, P801, J GEN VIROL

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Patterns of Persistent Viral Infections (Medical Progress)

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CITED REFERENCES
1. Fenner F, White DO. Medical virology. 2nd ed. New York: Academic Press, 1976:140-61.
2. ter Meulen V, Hall WW. Slow virus infections of the nervous system: virological, immunological and pathogenetic considerations. J Gen Virol 1978; 41:1-25.
3. Mims CA. Role of persistence in viral pathogenesis. In: Mahy BWJ, Minson AC, Darby GK, eds. Viral persistence. London: Cambridge University Press, 1982:1-13.
4. Stroop WG, Baringer JR. Persistent, slow and latent viral infections. Prog Med Virol 1982; 28:1-43.
5. Norden CW, Kuller LH. Identifying infectious etiologies of chronic disease. Rev Infect Dis 1984; 6:200-13.
6. Ohmann HB, Babiuk LA. Viral infections in domestic animals as models for studies of viral immunology and pathogenesis. J Gen Virol 1986;

67:1-25.
7. Southern P, Oldstone MBA. Medical consequences of persistent viral infection. N Engl J Med 1986; 314:359-67.
8. Haywood AM. Persistent viral infections. In: Kelley VC, ed. Practice of pediatrics. Philadelphia: JB Lippincott (in press).
9. Haywood AM, Valenti WM, Strike DG. Papovavirus and retrovirus infection. In: Kelley VC, ed. Practice of pediatrics. Philadelphia: JB Lippincott (in press).
10. Kimberlin RH. Problems of long incubation viral diseases and their eradication. In: Haresign W, ed. Sheep production. London: Butterworths, 1983:299-316.
11. Sigurdsson B. Rida, a chronic encephalitis of sheep: with general remarks on infections which develop slowly and some of their special characteristics. Br Vet J 1954; 110:341-54.
12. Johnson RT. Viruses and chronic neurological diseases. Johns Hopkins Med J 1982; 150:132-40.
13. Rawls WE. Viral persistence in congenital rubella. Prog Med Virol 1974; 18:273-88.
14. Oldstone MBA. Viruses can alter cell function without causing cell pathology: disordered function leads to imbalance of homeostasis and disease. In: Notkins AL, Oldstone MBA, eds. Concepts in viral pathogenesis. New York: Springer-Verlag, 1984:269-76.
15. Oldstone MBA. Immunopathology of persistent viral infections. Hosp Pract 1982; 17(12):61-72.
16. Porter DD, Cho HJ. Aleutian disease of mink: a model for persistent infection. In: Fraenkel-Conrat H, Wagner RR, eds. Comprehensive virology. Vol. 16. New York: Plenum Press, 1980:233-56.
17. Kilham L, Margolis G. Problems of human concern arising from animal models of intrauterine and neonatal infections due to viruses: a review. I. Introduction and virologic studies. Prog Med Virol 1975; 20:113-43.
18. Friedmann A, Lorch Y. Theiler's virus infection: a model for multiple sclerosis. Prog Med Virol 1985; 31:43-83.
19. Fabricant CG. Herpesvirus-induced atherosclerosis. In: Notkins AL, Oldstone MBA, eds. Concepts in viral pathogenesis. New York: Springer-Verlag, 1984:248-53.
20. Wege H, Siddell S, ter Meulen V. The biology and pathogenesis of coronaviruses. Curr Top Microbiol Immunol 1982; 99:165-200.
21. Rott R, Herzog S, Fleischer B, et al. Detection of serum antibodies to Borna disease virus in patients with psychiatric disorders. Science 1985; 228:755-6.
22. Kimberlin RH. Scrapie: the disease and the infectious agent. TINS 1984; 7:312-6.
23. Gardner MB. Retroviral spongiform polioencephalomyelopathy. Rev Infect Dis 1985; 7:99-110.
24. Robinson HL, Miles BD. Avian leukosis virus-induced osteopetrosis is associated with the persistent synthesis of viral DNA. Virology 1985; 141:130-43.
25. Lowy DR. Transformation and oncogenesis: retroviruses. In: Fields BN, Knipe DM, Chanock RM, Melnick JL, Roizman B, Shope RE, eds. Virology. New York: Raven Press, 1985:235-63.
26. Cheevers WP, McGuire TC. Equine infectious anemia virus: immunopathogenesis and persistence. Rev Infect Dis 1985; 7:83-8.
27. Nathanson N, Georgsson G, Palsson PA, Najjar JA, Lutley R, Petursson G. Experimental visna in Icelandic sheep: the prototype lentiviral infection. Rev Infect Dis 1985; 7:75-82.
28. Narayan O, Cork LC. Lentiviral diseases of sheep and goats: chronic pneumonia leukoencephalomyelitis and arthritis. Rev Infect Dis 1985; 7:89-98.
29. McGuire TC. Retrovirus-induced arthritis. In: Notkins AL, Oldstone MBA,

eds. Concepts in viral pathogenesis. New York: Springer-Verlag, 1984:254-9.
30. Green M. Transformation and oncogenesis: DNA viruses. In: Fields BN, Knipe DM, Chanock RM, Melnick JL, Roizman B, Shope RE, eds. Virology. New York: Raven Press, 1985:183-234.
31. Gajdusek DC. Unconventional viruses and the origin and disappearance of kuru. Science 1977; 197:943-60.
32. Merz PA, Rohwer RG, Kascsak R, et al. Infection-specific particle from the unconventional slow virus diseases. Science 1984; 225:437-40.
33. Prusiner SB. Novel proteinaceous infectious particles cause scrapie. Science 1982; 216:136-44.
34. Prusiner SB, Groth DF, Bolton DC, Kent SB, Hood LE. Purification and structural studies of a major scrapie prion protein. Cell 1984; 38:127-34.
35. Diringer H, Gelderblom H, Hilmert H, Ozel M, Edelbluth C, Kimberlin RH. Scrapie infectivity, fibrils and low molecular weight protein. Nature 1983; 306:476-8.
36. Manuelidis L, Valley S, Manuelidis EE. Specific proteins associated with Creutzfeldt-Jakob disease and scrapie share antigenic and carbohydrate determinants. Proc Natl Acad Sci USA 1985; 82:4263-7.
37. Bockman JM, Kingsbury DT, McKinley MP, Bendheim PE, Prusiner SB. Creutzfeldt-Jakob disease prion proteins in human brains. N Engl J Med 1985; 312:73-8.
38. Gibbs CJ Jr, Joy A, Heffner R, et al. Clinical and pathological features and laboratory confirmation of Creutzfeldt-Jakob disease in a recipient of pituitary-derived human growth hormone. N Engl J Med 1985; 313:734-8.
39. Oesch B, Westaway D, Walchli M, et al. A cellular gene encodes scrapie PrP 27-30 protein. Cell 1985; 40:735-46.
40. Wietgrefe S, Zupancic M, Haase A, et al. Cloning of a gene whose expression is increased in scrapie and in senile plaques in human brain. Science 1985; 230:1177-9.
41. Rohwer RG. Scrapie infectious agent is virus-like in size and susceptibility to inactivation. Nature 1984; 308:658-62.
42. Dees C, McMillan BC, Wade WF, German TL, Marsh RF. Characterization of nucleic acids in membrane vesicles from scrapie-infected hamster brain. J Virol 1985; 55:126-32.
43. Prusiner SB. Human slow infections-prion diseases. In: Zuckerman AJ, Banatvala JE, Pattison JR, eds. Principles and practice of clinical virology. London: John Wiley, 1986:545-65.
44. Brown P, Cathala F, Castaigne P, Gajdusek DC. Creutzfeldt-Jakob disease: clinical analysis of a consecutive series of 230 neuropathologically-verified cases. Ann Neurol (in press).
45. Masters CL, Gajdusek DC, Gibbs CJ Jr. Creutzfeldt-Jakob disease virus isolations from the Gerstmann-Straussler syndrome: with an analysis of the various forms of amyloid plaque deposition in the virus-induced spongiform encephalopathies. Brain 1981; 104:559-88.
46. Degenerative neurologic disease in patients formerly treated with human growth hormone: report of the Committee on Growth Hormone Use of the Lawson Wilkins Pediatric Endocrine Society. J Pediatr 1985; 107:10-2.
47. Brown P, Gajdusek DC, Gibbs CJ Jr, Asher DM. Potential epidemic of Creutzfeldt-Jakob disease from human growth hormone therapy. N Engl J Med 1985; 313:728-31.
48. Hanshaw JB, Dudgeon JA, Marshall WC. Viral diseases of the fetus and newborn. 2nd ed. Philadelphia: WB Saunders, 1985:13-91.
49. Robinson WS. Hepatitis B virus and the delta agent. In: Mandell GL, Douglas RG Jr, Bennett JE, eds. Principles and practice of infectious diseases. 2nd ed. New York: John Wiley, 1985:1002-29.
50. Rawls WE. Herpes simplex virus. In: Fields BN, Knipe DM, Chanock RM, Melnick JL, Roizman B, Shope RE, eds. Virology. New York: Raven Press,

1985:527-61.
51. Takahashi M. Chickenpox virus. Adv Virus Res 1983; 28:285-356.
52. Ho M. Cytomegalovirus. In: Mandell GL, Douglas RG Jr, Bennett JE, eds. Principles and practice of infectious diseases. 2nd ed. New York: John Wiley, 1985:960-70.
53. Miller G. Epstein-Barr virus. In: Fields BN, Knipe DM, Chanock RM, Melnick JL, Roizman B, Shope RE, eds. Virology. New York: Raven Press, 1985:563-89.
54. Snavely SR, Liu C. Adenoviruses. In: Belshe RB, ed. Textbook of human virology. Littleton, Mass.: PSG, 1984:779-94.
55. Shah KV. Papovaviruses. In: Fields BN, Knipe DM, Chanock RM, Melnick JL, Roizman B, Shope RE, eds. Virology. New York: Raven Press, 1985:371-91.
56. Pfister H. Biology and biochemistry of papillomaviruses. Rev Physiol Biochem Pharmacol 1984; 99:111-81.
57. Walker DL, Padgett BL. Progressive multifocal leukoencephalopathy. In: Fraenkel-Conrat H, Wagner RR, eds. Virus-host interactions: receptors, persistence, and neurological diseases. (Comprehensive virology. Vol. 18). New York: Plenum Press, 1983:161-93.
58. Rosen S, Harmon W, Krensky AM, et al. Tubulo-interstitial nephritis associated with polyomavirus (BK type) infection. N Engl J Med 1983; 308:1192-6.
59. ter Meulen V, Stephenson JR, Kreth HW. Subacute sclerosing panencephalitis. In: Fraenkel-Conrat H, Wagner RR, eds. Virus-host interactions: receptors, persistence, and neurological diseases. (Comprehensive virology. Vol. 18). New York: Plenum Press, 1983:105-59.
60. Bell WE, McCormick WF. Neurologic infections in children. 2nd ed. Philadelphia: WB Saunders 1981:468-92.
61. Broder S, Bunn PA Jr, Jaffe ES, et al. T-cell lymphoproliferative syndrome associated with human T-cell leukemia/lymphoma virus. Ann Intern Med 1984; 100:543-57.
62. Kalyanaraman VS, Sarngadharan MG, Robert-Guroff M, et al. A new subtype of human T-cell leukemia virus (HTLV-II) associated with a T-cell variant of hairy cell leukemia. Science 1982; 218:571-3.
63. Brown F. Human immunodeficiency virus. Science 1986; 232:1486.
64. Fauci AS, Masur H, Gelmann EP, Markham PD, Hahn BH, Lane HC. The acquired immunodeficiency syndrome: an update. Ann Intern Med 1985; 102:800-13.
65. Curran JW, Morgan WM, Hardy AM, Jaffe HW, Darrow WW, Dowdle WR. The epidemiology of AIDS: current status and future prospects. Science 1985; 229:1352-7.
66. Callahan R, Chiu I-M, Wong JFH, et al. A new class of endogenous human retroviral genomes. Science 1985; 228:1208-11.
67. Panem S. C-type virus expression in the placenta. Curr Top Pathol 1979; 66:175-89.
68. Kantor JA, Lee Y-H, Chirikjian JG, Feller WF. DNA polymerase with characteristics of reverse transcriptase purified from human milk. Science 1979; 204:511-3.
69. Howard CR, ed. New developments in practical virology. New York: Alan R Liss, 1982.
70. Link H, Panelius M, Salmi AA. Immunoglobulins and measles antibodies in subacute sclerosing panencephalitis: demonstration of synthesis of oligoclonal IgG with measles antibody activity within the central nervous system. Arch Neurol 1973; 28:23-30.
71. Tibbling G, Link H, Ohman S. Principles of albumin and IgG analyses in neurological disorders. I. Establishment of reference values. Scand J Clin Lab Invest 1977; 37:385-90.
72. Tourtellotte WW, Potvin AR, Fleming JO, et al. Multiple sclerosis: measurement and validation of central nervous system IgG synthesis

rate. Neurology (NY) 1980; 30:240-4.
73. Rudick RA. Humoral immunity in multiple sclerosis: clinical and investigative aspects. Semin Neurol 1985; 5:107-16.
74. Miller JR, Burke AM, Bever CT. Occurrence of oligoclonal bands in multiple sclerosis and other CNS diseases. Ann Neurol 1983; 13:53-8.
75. Baringer JR, Swoveland P. Recovery of herpes-simplex virus from human trigeminal ganglions. N Engl J Med 1973; 288:648-50.
76. Bornkamm GW, Desgranges C, Gissmann L. Nucleic acid hybridization for the detection of viral genomes. Curr Top Microbiol Immunol 1983; 104:287-98.
77. Kulski JK, Norval M. Nucleic acid probes in diagnosis of viral disease of man: brief review. Arch Virol 1985; 83:3-15.
78. Engleberg NC, Eisenstein BI. The impact of new cloning techniques on the diagnosis and treatment of infectious diseases. N Engl J Med 1984; 311:892-901.
79. Peden K, Mounts P, Hayward GS. Homology between mammalian cell DNA sequences and human herpesvirus genomes detected by a hybridization procedure with high-complexity probe. Cell 1982; 31:71-80.
80. Howley PM, Israel MA, Law M-F, Martin MA. A rapid method for detection and mapping homology between heterologous DNAs: evaluation of polyomavirus genomes. J Biol Chem 1979; 254:4876-83.
81. Haase A, Brahic M, Stowring L, Blum H. Detection of viral nucleic acids by in situ hybridization. Methods in virology. Vol. 7. New York: Academic Press, 1984:189-226.
82. Holland J, Spindler K, Horodyski F, Grabau E, Nichol S, VandePol S. Rapid evolution of RNA genomes. Science 1982; 215:1577-85.
83. Wong-Staal F, Shaw GM, Salahuddin SZ, et al. Genomic diversity of human T-lymphotropic virus type III (HTLV-III). Science 1985; 229:759-62.
84. Parrish CR, O'Connell PH, Evermann JF, Carmichael LE. Natural variation of canine parvovirus. Science 1985; 230:1046-8.
85. Khoury G, Gruss P. Enhancer elements. Cell 1983; 33:313-4.
86. Marx JL. More about the HTLV's and how they act. Science 1985; 229:37-8.
87. Byington DP, Johnson KP. Experimental subacute sclerosing panencephalitis in the hamster: correlation of age with chronic inclusion-cell encephalitis. J Infect Dis 1982; 126:18-26.
88. Rawls WE, Chan MA, Gee SR. Mechanisms of persistence in arenavirus infections: a brief review. Can J Microbiol 1981; 27:568-74.
89. Bittner JJ. Some possible effects of nursing on mammary gland tumor incidence in mice. Science 1936; 84:162.
90. Lawrence RA. Breast-feeding: a guide for the medical profession. 2nd ed. St. Louis: CV Mosby, 1985.
91. Dworsky M, Yow M, Stagno S, Pass RF, Alford C. Cytomegalovirus infection of breast milk and transmission in infancy. Pediatrics 1983; 72:295-9.
92. Ziegler JB, Cooper DA, Johnson RO, Gold J. Postnatal transmission of AIDS-associated retrovirus from mother to infant. Lancet 1985; 1:896-8.
93. Parry HB. Elimination of natural scrapie in sheep by sire genotype selection. Nature 1979; 277:127-9.
94. Brinton MA, Nathanson N. Genetic determinants of virus susceptibility: epidemiologic implications of murine models. Epidemiol Rev 1981; 3:115-39.
95. Dickinson AG, Fraser H. Scrapie: pathogenesis in inbred mice: an assessment of host control and response involving many strains of agent. In: ter Meulen V, Katz M, eds. Slow virus infections of the central nervous system. New York; Springer-Verlag 1977:3-14.
96. Kingsbury DT, Kasper KC, Stites DP, Watson JD, Hogan RN, Prusiner SB. Genetic control of scrapie and Creutzfeldt-Jakob disease in mice. J Immunol 1983; 131:491-6.

97. Fujinami RS, Oldstone MBA. Antibody initiates virus persistence: immune modulation and measles virus infection. In: Notkins AL, Oldstone MBA, eds. Concepts in viral pathogenesis. New York: Springer-Verlag, 1984:187-93.
98. Seligmann M, Chess L, Fahey JL, et al. AIDS -- an immunologic reevaluation. N Engl J Med 1984; 311:1286-92.
99. Peluso R, Haase A, Stowring L, Edwards M, Ventura P. A Trojan horse mechanism for the spread of visna virus in monocytes. Virology 1985; 147:231-6. 100. Casali P, Oldstone MBA. Immune complexes in viral infection. Curr Top Microbiol Immunol 1983; 104:7-48. 101. Johnson RT. Viral infections of the nervous system. New York: Raven Press, 1982. 102. Rovner DM, Weiner LP. Chronic viral disease of myelin. Semin Neurol 1985; 5:168-79. 103. Mims CA, Cuzner ML, Kelly RE, eds. Viruses and demyelinating diseases. London: Academic Press, 1983. 104. Masters CL, Gajdusek DC, Gibbs CJ Jr. The familial occurrence of Creutzfeldt-Jakob disease and Alzheimer's disease. Brain 1981; 104:535-58. 105. Notkins AL, Onodera T, Prabhakar B. Virus-induced autoimmunity. In: Notkins AL, Oldstone MBA, eds. Concepts in viral pathogenesis. New York: Springer-Verlag, 1984:210-5. 106. Fujinami RS, Oldstone MBA, Wroblewska Z, Frankel ME, Koprowski H. Molecular mimicry in virus infection: crossreaction of measles virus phosphoprotein or of herpes simplex virus protein with human intermediate filaments. Proc Natl Acad Sci USA 1983; 80:2346-50. 107. Johnson RT, Griffin DE, Gendelman HE. Postinfectious encephalomyelitis. Semin Neurol 1985; 5:180-90. 108. Ahmed R, Oldstone MBA. Mechanisms and biological implications of virus-induced polyclonal B-cell activation. In Notkins AL, Oldstone MBA, eds. Concepts in viral pathogenesis. New York: Springer-Verlag, 1984:231-8. 109. Jahnke U, Fischer EH, Alvord EC Jr. Sequence homology between certain viral proteins and proteins related to encephalomyelitis and neuritis. Science 1985; 229:282-4. 110. Gocke DJ. Extrahepatic manifestations of viral hepatitis. Am J Med Sci 1975; 270:49-52. 111. Sever JL, South MA, Shaver KA. Delayed manifestations of congenital rubella. Rev Infect Dis 1985; 7:Suppl 1:S164-S169. 112. Bennett JC. The etiology of rheumatoid arthritis. In: Kelley WN, Harris ED Jr, Rudy S, Sledge CB, eds. Textbook of rheumatology. Philadelphia: WB Saunders, 1985:879-86. 113. Simpson RW, McGinty L, Simon L, Smith CA, Godzeski CW, Boyd RJ. Association of parvoviruses with rheumatoid arthritis of humans. Science 1984; 223:1425-8. 114. Kurtzke JF, Hyllested K. Multiple sclerosis in the Faroe Islands. I. Clinical and epidemiological features. Ann Neurol 1979; 5:6-21. 115. Waksman BH, Reynolds WE. Multiple sclerosis as a disease of immune regulation. Proc Soc Exp Biol Med 1984; 175:282-94. 116. Weiss RA. Unravelling the complexities of carcinogenesis. In: Rigby PWJ, Wilkie NM, eds. Viruses and cancer. Cambridge: Cambridge University Press, 1985:1-21. 117. Hayward WS, Neel BG, Astrin SM. Activation of a cellular onc gene by promoter insertion in ALV-induced lymphoid leukosis. Nature 1981; 290:475-80. 118. de-The G. Is Burkitt's lymphoma related to perinatal infection by Epstein-Barr virus? Lancet 1977; 1:335-8. 119. Nishioka K. Hepatitis B virus and hepatocellular carcinoma: postulates for an etiological relationship. Adv Viral Oncol 1985; 5:173-99.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

?e au=berman, philip w.

Ref	Items	Index-term
E1	2	*AU=BERMAN, PHILIP W.
E2	1	AU=BERMAN, PHILIPP W.
E3	8	AU=BERMAN, PHILLIP
E4	16	AU=BERMAN, PHILLIP M.
E5	41	AU=BERMAN, PHILLIP W.
E6	2	AU=BERMAN, PHILLIP WAYNE

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E7         3  AU=BERMAN, PHYLLIS M.
E8        42  AU=BERMAN, R.
E9         1  AU=BERMAN, R. A.
E10        9  AU=BERMAN, R. F.
E11       10  AU=BERMAN, R. G.
E12        1  AU=BERMAN, R. H.

          Enter P or PAGE for more
?s e1
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>>>  or undefined in one or more files.
      S9       2  AU="BERMAN, PHILIP W."
?rd
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     S10       2  RD (unique items)
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 10/5/1     (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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  121032740    CA: 121(3)32740z    JOURNAL
  Comparison of the immune response to recombinant gp120 in humans and
chimpanzees
  AUTHOR(S): Berman, Philip W.; Eastman, Donna J.; Wilkes, Denise M.;
Nakamura, Gerald R.; Gregory, Timothy J.; Schwartz, David; Gorse, Geoffrey;
Belshe, Robert; Clements, Mary Lou; et al.
  LOCATION: Dep. Immunol., South San Francisco, CA, 94080, USA
  JOURNAL: AIDS (London)  DATE: 1994  VOLUME: 8  NUMBER: 5  PAGES: 591-601
  CODEN: AIDSET  ISSN: 0269-9370  LANGUAGE: English
  SECTION:
CA215002 Immunochemistry
  IDENTIFIERS: antibody gp120 glycoprotein chimpanzee HIV, human
immunodeficiency virus antibody gp120 glycoprotein
  DESCRIPTORS:
Sialoglycoproteins,gp120env...
    antibodies in chimpanzee and humans to recombinant, of HIV-1IIIB,
    comparison of
Acquired immune deficiency syndrome...
    antibody response to recombinant HIV gp120 glycoprotein in humans and
    chimpanzee in relation to
Vaccines...
    for human immunodeficiency virus, antibody response to recombinant
    gp120 glycoprotein in humans and chimpanzee in relation to
Virus,animal, human immunodeficiency 1...
    gp120 glycoprotein of, antibodies in chimpanzee and humans to
    recombinant, comparison of
Antigens,CD4...
    gp120 glycoprotein of HIV-1IIIB binding to, recombinant protein-induced
    human and chimpanzee antibodies inhibition of
Antibodies,crossreacting... Antibodies,neutralizing...
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to HIV-1 strains, recombinant gp120 glycoprotein induction of, in humans and chimpanzee
Antibodies...
to recombinant gp120 glycoprotein of HIV-1IIIB, in humans and chimpanzee, avidity and half-life for

10/5/2 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

106212415 CA: 106(25)212415w JOURNAL
Native and recombinant herpes simplex virus type 1 envelope proteins induce human immune T-lymphocyte resonances
AUTHOR(S): Torseth, John W.; Cohen, Gary H.; Eisenberg, Roselyn J.; Berman, Philip W.; Lasky, Larry A.; Cerini, Costantino P.; Heilman, Conrad J.; Kerwar, Somesh; Merigan, Thomas C.
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JOURNAL: J. Virol. DATE: 1987 VOLUME: 61 NUMBER: 5 PAGES: 1532-9
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SECTION:
CA215010 Immunochemistry
IDENTIFIERS: herpes simplex virus glycoprotein T lymphocyte
DESCRIPTORS:
Lymphokines and Cytokines,interleukin 2...
formation of, herpes simplex virus type 1 envelope proteins induction of, in humans
Interferons,.gamma.-...
formation of, herpes simplex virus type 1 envelope proteins stimulation of, in humans
Glycoproteins,specific or class, gB... Glycoproteins,specific or class, gC ... Glycoproteins,specific or class, gD...
from herpes simplex virus type 1 envelope, lymphokines and helper T-lymphocyte stimulation by, in humans
Virus,animal, herpes simplex 1...
glycoproteins of envelope of, lymphokines and helper T-lymphocytes stimulation by, in humans
Lymphocyte,T-, helper...
herpes simplex virus type 1 envelope proteins stimulation of, of humans
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Set	Items	Description
S1	92464	HERPES(4W)SIMPLEX(4W)VIRUS
S2	92464	HERPES(4W)SIMPLEX(4W)VIRUS
S3	3212	VACCINE AND S2
S4	252753	POLYPEPTIDE
S5	68983	MEMBRANE(4W)BOUND
S6	100	S3 AND S4
S7	10	S6 AND S5
S8	7	RD (unique items)
S9	2	AU="BERMAN, PHILIP W."
S10	2	RD (unique items)

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>>>Duplicate detection is not supported for File 337.
>>>Duplicate detection is not supported for File 340.

>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 350.
>>>Duplicate detection is not supported for File 351.
>>>Duplicate detection is not supported for File 456.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S12 6 RD (unique items)
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12/5/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11478401 BIOSIS Number: 98078401
Expression and characterization of baculovirus expressed herpes simplex virus type 1 glycoprotein L
Ghiasi H; Kaiwar R; Slanina S; Nesburn A B; Wechsler S L
Ophthalmol. Res., Davis Bldg. Rm 5072, Cedars-Sinai Med. Cent., 8700 Beverly Blvd., Los Angeles, CA 90048, USA
Archives of Virology 138 (3-4). 1994. 199-212.
Full Journal Title: Archives of Virology
ISSN: 0304-8608
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 004 Ref. 048811
We have constructed a recombinant baculovirus expressing high levels of the herpes simplex virus type 1 (HSV-1) glycoprotein L (gL) in Sf9 cells. Sf9 cells infected with this recombinant virus synthesized three polypeptides of 26-27 kDa 28 kDa, and 31 kDa. The 28 and 31 kDa species were sensitive to tunicamycin and N-glycosidase F (PNGase F) treatment, suggesting that they were glycosylated. As shown by both indirect immunofluorescence and Western blot analysis, using polyclonal antibodies to synthetic gL peptides indicated that the baculovirus expressed gL was abundant on the surface of baculovirus gL infected Sf9 cells. A small fraction of the 31 kDa polypeptide was secreted into the extracellular medium as judged by Western blot analysis. The secreted form of gL was completely resistant to Endoglycosidase H (Endo-H), while the membrane associated form of gL was only partially resistant to Endo-H treatment, suggesting that the secreted gL represented a subpopulation of the membrane bound gL. Mice vaccinated with baculovirus expressed gL produced serum antibodies that reacted with authentic HSV-1 gL. However, these mice produced no HSV-1 neutralizing antibody (titer lt 1: 10) and they were not protected from lethal intraperitoneal or lethal ocular challenge with HSV-1. Thus, when used as a vaccine in the mouse model, gL, similar to our findings with HSV-1 gH, but unlike our results with the other 6 HSV-1 glycoproteins that we have expressed in this baculovirus system, did not provide any protection against HSV-1 challenge.
Descriptors/Keywords: RESEARCH ARTICLE; MOUSE; SF9 CELLS; GLYCOSYLATION; SURFACE EXPRESSION; SECRETION; VACCINE SUITABILITY; CHALLENGE PROTECTION; GENETIC ENGINEERING
Concept Codes:
*10064 Biochemical Studies-Proteins, Peptides and Amino Acids
*10068 Biochemical Studies-Carbohydrates
*10508 Biophysics-Membrane Phenomena
*13004 Metabolism-Carbohydrates
*13012 Metabolism-Proteins, Peptides and Amino Acids
*22018 Pharmacology-Immunological Processes and Allergy
*31500 Genetics of Bacteria and Viruses
*33506 Virology-Animal Host Viruses
*34504 Immunology and Immunochemistry-Bacterial, Viral and Fungal

*36006 Medical and Clinical Microbiology-Virology
*64076 Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology
Biosystematic Codes:
02603 Baculoviridae (1993-)
02612 Herpesviridae (1993-)
75330 Lepidoptera
86375 Muridae
Super Taxa:
Microorganisms; Viruses; Animals; Invertebrates; Arthropods; Insects; Chordates; Vertebrates; Nonhuman Vertebrates; Mammals; Nonhuman Mammals ; Rodents

12/5/2 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

11847825 PASCAL No.: 95-0010546
Expression and characterizatoin of baculovirus expressed herpes simplex virus type 1 glycoprotein L
GHIASI H; KAIWAR R; SLANINA S; BESBURN A B; WECHSLER S L
UCLA, school medicine, ophthalmology res., Los Angeles CA 90048, USA
Journal: Archives of virology, 1994, 138 (3-4) 199-212
ISSN: 0304-8608 Availability: INIST-6355; 354000042419320020
No. of Refs.: 22 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: Austria
Language: English
We have constructed a recombinant baculovirus expressing high levels of the herpes simplex virus type 1 (HSV-1) glycoprotein L (gL) in Sf9 cells. Sf9 cells infected with this recombinant virus synthesized three polypeptides of 2627 kDa 28 kDa, and 31 kDa. The 28 and 31 kDa species were sensitive to tunicamycin and N-glycosidase F (PNGase F) treatment, suggesting that they were glycosylated. As shown by both indirect immunofluorescence and Western blot analysis, using polyclonal antibodies to synthetic gL peptides indicated that the baculovirus expressed gL was abundant on the surface of baculovirus gL infected Sf9 cells. A small fraction of the 31 kDa polypeptide was secreted into the extracellular medium as judged by Western blot analysis

English Descriptors: Herpesvirus hominis 1; Nuclear polyhedrosis virus; Recombinant protein; Gene expression; Vaccine; Immunogenicity; Antigenicity; Mouse
Broad English Descriptors: Alphaherpesvirinae; Herpesviridae; Virus; Baculovirus; Baculoviridae; Rodentia; Mammalia; Vertebrata

French Descriptors: Herpesvirus hominis 1; Virus polyedrose nucleaire; Proteine recombinante; Expression genique; Vaccin; Immunogenicite; Antigenicite; Souris; Glycoproteine L

Classification Codes: 002A05C07

12/5/3 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09344285 95274285

Expression of membrane-bound and secreted forms of equine herpesvirus 1 glycoprotein D by recombinant baculovirus.
Flowers CC; Flowers SP; Sheng Y; Tarbet EB; Jennings SR; O'Callaghan DJ
Department of Microbiology and Immunology, Louisiana State University Medical Center, Shreveport 71130-3932, USA.
Virus Res (NETHERLANDS) Jan 1995, 35 (1) p17-34, ISSN 0168-1702 Journal Code: X98
Contract/Grant No.: AI 22001, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9508
Subfile: INDEX MEDICUS
Analyses of the synthesis and processing of recombinant full-length glycoprotein D of equine herpesvirus type 1 (EHV-1; gD392) or recombinant truncated gD (gD352) expressed in baculovirus-infected Sf9 cells revealed the following: (1) gD polypeptides encoded by both recombinant baculoviruses react with gD-specific antibodies including peptide-specific antiserum that neutralizes EHV-1 in a plaque reduction assay, (2) both the full-length recombinant gD392 and the truncated gD352 are expressed predominantly as gD species that contain high mannose-type oligosaccharides (55 kDa and 52 kDa, respectively), (3) both the full-length recombinant gD392 and the truncated gD352 are also expressed in lesser amounts as gD species that contain complex-type oligosaccharides (58 kDa and 55 kDa, respectively) as well as the unglycosylated forms of gD (43 kDa and 37 kDa, respectively), (4) flow cytometric analyses of cells expressing gD392 revealed that gD first appears on the cell surface at 24 h post infection; by 60 h, 95% of the cells express high levels of cell surface gD, (5) cells expressing gD352, in contrast to cells expressing gD392, secrete gD into the extracellular medium. This initial demonstration that immunoreactive EHV-1 glycoprotein D can be produced as a secreted polypeptide in the baculovirus system should provide reagents to assess the potential use of gD as a subunit vaccine in an animal model.
Tags: Animal; Comparative Study; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: *Genetic Vectors--Genetics--GE; *Herpesvirus 1, Equid --Genetics--GE; *Membrane Proteins--Biosynthesis--BI; *Nuclear Polyhedrosis Virus--Genetics--GE; *Recombinant Fusion Proteins--Biosynthesis--BI; *Viral Envelope Proteins--Biosynthesis--BI; Antibodies, Viral--Immunology--IM; Cell Line; Glycosylation; Herpesvirus 1, Equid--Immunology--IM; Membrane Proteins--Genetics--GE; Membrane Proteins--Immunology--IM; Oligosaccharides--Analysis--AN; Protein Processing, Post-Translational; Recombinant Fusion Proteins--Immunology--IM; Recombinant Fusion Proteins--Secretion--SE; Spodoptera; Viral Envelope Proteins--Genetics--GE; Viral Envelope Proteins --Immunology--IM; Viral Envelope Proteins--Secretion--SE
CAS Registry No.: 0 (glycoprotein D, herpes simplex virus type 1); 0 (Antibodies, Viral); 0 (Genetic Vectors); 0 (Membrane Proteins); 0 (Oligosaccharides); 0 (Recombinant Fusion Proteins); 0 (Viral Envelope Proteins)

12/5/4 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R)

13663171 Genuine Article#: QF404 Number of References: 27
Title: EXPRESSION OF MEMBRANE-BOUND AND SECRETED FORMS OF EQUINE HERPESVIRUS-1 GLYCOPROTEIN-D BY RECOMBINANT BACULOVIRUS
Author(s): FLOWERS CC; FLOWERS SP; SHENG YW; TARBET EB; JENNINGS SR; OCALLAGHAN DJ
Corporate Source: LOUISIANA STATE UNIV,MED CTR,DEPT MICROBIOL &

IMMUNOL,1501 KINGS HIGHWAY/SHREVEPORT//LA/71130; LOUISIANA STATE UNIV,MED CTR,DEPT MICROBIOL & IMMUNOL/SHREVEPORT//LA/71130
Journal: VIRUS RESEARCH, 1995, V35, N1 (JAN), P17-34
ISSN: 0168-1702
Language: ENGLISH Document Type: ARTICLE
Geographic Location: USA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: VIROLOGY
Abstract: Analyses of the synthesis and processing of recombinant full-length glycoprotein D of equine herpesvirus type 1 (EHV-1; gD392) or recombinant truncated go (gD352) expressed in baculovirus-infected Sf9 cells revealed the following: (1) go polypeptides encoded by both recombinant baculoviruses react with go-specific antibodies including peptide-specific antiserum that neutralizes EHV-1 in a plaque reduction assay, (2) both the full-length recombinant gD392 and the truncated gD352 are expressed predominantly as go species that contain high mannose-type oligosaccharides (55 kDa and 52 kDa, respectively), (3) both the full-length recombinant gD392 and the truncated gD352 are also expressed in lesser amounts as go species that contain complex-type oligosaccharides (58 kDa and 55 kDa, respectively) as well as the unglycosylated forms of go (43 kDa and 37 kDa, respectively), (4) flow cytometric analyses of cells expressing gD392 revealed that go first appears on the cell surface at 24 h post infection; by 60 h, 95% of the cells express high levels of cell surface go, (5) cells expressing gD352, in contrast to cells expressing gD392, secrete go into the extracellular medium. This initial demonstration that immunoreactive EHV-1 glycoprotein D can be produced as a secreted polypeptide in the baculovirus system should provide reagents to assess the potential use of go as a subunit vaccine in an animal model.
Descriptors--Author Keywords: EQUINE HERPESVIRUS TYPE 1 ; GLYCOPROTEIN D ; BACULOVIRUS ; SECRETED GD
Identifiers--KeyWords Plus: SIMPLEX VIRUS TYPE-1; UNIQUE SHORT SEGMENT; D GENE; SEQUENCE-ANALYSIS; HOMOLOG; IDENTIFICATION; VECTORS; GENOME
Research Fronts: 93-2767 002 (BACULOVIRUS EXPRESSION SYSTEM; INSECT CELLS; AUTOGRAPHA-CALIFORNICA NUCLEAR POLYHEDROSIS-VIRUS; RECOMBINANT VIRAL INSECTICIDES)
93-0591 001 (HERPES-SIMPLEX VIRUS TYPE-1; TRANSPORT CAPSID ASSEMBLY PROTEIN (TP CAP) GENE; EXHIBIT ALTERED VIRAL THYMIDINE KINASE EXPRESSION)
Cited References:
ALLEN GP, 1987, V61, P2454, J VIROL
AUDONNET JC, 1990, V71, P2969, J GEN VIROL
COHEN GH, 1984, V49, P102, J VIROL
DENHURK SVL, 1991, V65, P263, J VIROL
EISENBERG RJ, 1982, V56, P1014, J VIROL
ELDER JH, 1982, V79, P4540, P NATL ACAD SCI USA
ELTON DM, 1992, V73, P1227, J GEN VIROL
FLOWERS CC, 1992, V66, P6451, J VIROL
FLOWERS CC, 1991, V180, P175, VIROLOGY
FLOWERS CC, 1992, V190, P307, VIROLOGY
GHIASI H, 1991, V121, P163, ARCH VIROL
GHIASI H, 1994, V68, P2118, J VIROL
KRISHNA S, 1989, V70, P1805, J GEN VIROL
LANDOLFI V, 1993, V11, P407, VACCINE
LASKY LA, 1984, V2, P527, BIO-TECHNOL
LOVE DN, 1993, V67, P6820, J VIROL
LOVE DN, 1992, V30, P387, VET MICROBIOL
LUCKOW VA, 1988, V6, P47, BIOTECHNOLOGY
MILLER LK, 1988, V42, P177, ANNU REV MICROBIOL
MUGGERIDGE MI, 1990, V2, P459, IMMUNOCHEMISTRY VIRU

OCALLAGHAN DJ, 1968, V36, P104, VIROLOGY
SISK WP, 1994, V68, P766, J VIROL
SUMMERS MD, 1987, MANUAL METHODS BACUL
TELFORD EAR, 1992, V189, P304, VIROLOGY
THOMSEN DR, 1990, V43, P67, J CELL BIOCHEM
WHALLEY M, 1991, V5, P313, VIRUS GENES
WHITTAKER GR, 1992, V73, P801, J GEN VIROL

12/5/5 (Item 1 from file: 444)
DIALOG(R)File 444:NEJM Online

00108320

Mechanisms of Disease: The Molecular Biology Of Human Immunodeficiency Virus Type 1 Infection (Review Article)

Greene, Warner C.
The New England Journal of Medicine
Jan 31, 1991; 324 (5),pp 308-317
LINE COUNT: 00566 WORD COUNT: 07820
ISSN: 0028-4793
CORPORATE SOURCE: From the Department of Medicine, Howard Hughes Medical Institute, and the Department of Microbiology and Immunology, Duke University Medical Center, Durham, NC 27710, where reprint requests should be addressed to Dr. Greene.

CITED REFERENCES

1. Barre-Sinoussi F, Chermann JC, Rey F, et al Isolation of a T-lymphocyte retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 1983; 220:868-71.
2. Gallo RC, Salahuddin SZ, Popovic M, et al Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk of AIDS. Science 1984; 224:500-3.
3. AIDS Update 1990; 3(28):6-8.
4. Curran JW, Jaffe HW, Hardy AM, Morgan WM, Selik RM, Dondero TJ. Epidemiology of HIV infection and AIDS in the United States. Science 1988; 239:610-6.
5. Letvin NL. Animal models for AIDS. Immunol Today 1990; 11:322-6.
6. Varmus H. Retroviruses. Science 1988; 240:1427-35.
7. Gelderblom HR, Hausmann EHS, Ozel M, Pauli G, Koch MA. Fine structure of human immunodeficiency virus (HIV) and immunolocalization of structural proteins. Virology 1987; 156:171-6.
8. Fauci AS. The human immunodeficiency virus: infectivity and mechanisms of pathogenesis. Science 1988; 239:617-22.
9. Dalgleish AG, Beverley PCL, Clapham PR, Crawford DH, Greaves MF, Weiss RA. The CD4 (T4) antigen is an essential component of the receptor for the AIDS retrovirus. Nature 1984; 312:763-7.
10. Klatzmann D, Champagne E, Chamaret S, et al T-lymphocyte T4 molecule behaves as the receptor for human retrovirus LAV. Nature 1984; 312:767-8.
11. Smith DH, Byrn RA, Marsters SA, Gregory T, Groopman JE, Capon DJ. Blocking of HIV-1 infectivity by a soluble, secreted form of the CD4 antigen. Science 1987; 238:1704-7.
12. Fisher RA, Bertonis JM, Meier W, et al HIV infection is blocked in vitro by recombinant soluble CD4. Nature 1988; 331:76-8.
13. Daar ES, Li XL, Moudgil T, Ho DD. High concentrations of recombinant

soluble CD4 are required to neutralize primary human immunodeficiency virus type 1 isolates. Proc Natl Acad Sci U S A 1990; 87:6574-8.
14. Mitsuya H, Looney DJ, Kuno S, Ueno R, Wong-Staal F, Broder S. Dextran sulfate suppression of viruses in the HIV family: inhibition of virion binding to CD4(sup +) cells. Science 1988; 240:646-9.
15. Abrams DI, Kuno S, Wong R, et al Oral dextran sulfate (UA001) in the treatment of the acquired immunodeficiency syndrome (AIDS) and AIDS-related complex. Ann Intern Med 1989; 110:183-8.
16. Finberg RW, Diamond DC, Mitchell DB, et al Prevention of HIV-1 infection and preservation of CD4 function by the binding of CPFs to gpl20. Science 1990; 249:287-91.
17. Gartner S, Markovits P, Markovitz DM, Kaplan MH, Gallo RC, Popovic M. The role of mononuclear phagocytes in HTLV-III/LAV infection. Science 1986; 233:215-9.
18. Ho DD, Rota TR, Hirsch MS. Infection of monocyte/macrophages by human T lymphotropic viruses type III. J Clin Invest 1986; 77:1712-5.
19. Castro BA, Cheng-Mayer C, Evans LA, Levy JA. HIV heterogeneity and viral pathogenesis. AIDS 1988; 2:Suppl 1:S17-S27.
20. Fisher AG, Ensoli B, Looney D, et al Biologically diverse molecular variants within a single HIV-1 isolate. Nature 1988; 334:444-7.
21. York-Higgins D, Cheng-Mayer C, Bauer D, Levy JA, Dina D. Human immunodeficiency virus type 1 cellular host range, replication, and cytopathicity are linked to envelope region of the viral genome. J Virol 1990; 64:4016-20.
22. Cordonnier A, Montagnier L, Emerman M. Single amino-acid changes in HIV envelope affect viral tropism and receptor binding. Nature 1989; 340:571-4.
23. Maddon PJ, Dalgleish AG, McDougal JS, Clapham PR, Weiss RA, Axel R. The T4 gene encodes the AIDS virus receptor and is expressed in the immune system and the brain. Cell 1986; 47:333-48.
24. Stein BS, Gowda SD, Lifson JD, Penhallow RC, Bensch KG, Engleman EG. pH-independent HIV entry into CD4-positive T cells via virus envelope fusion to the plasma membrane. Cell 1987; 49:659-68.
25. Bedinger P, Moriarty A, von Borstel RC II, Donovan NJ, Steimer KS, Littman DR. Internalization of the human immunodeficiency virus does not require the cytoplasmic domain of CD4. Nature 1988; 334:162-5.
26. Veronese FD, DeVico AL, Copeland T, Oroszlan S, Gallo RC, Sarngadharan M. Characterization of gp41 as the transmembrane protein coded by the HTLV-III/LAV envelope gene. Science 1985; 229:1402-5.
27. Richardson CD, Choppin PW. Oligopeptides that specifically inhibit membrane fusion by paramyxoviruses: studies on the site of action. Virology 1983; 131:518-32.
28. Levy JA, Kaminsky LS, Morrow WJW, et al Infection by the retrovirus associated with the acquired immunodeficiency syndrome: clinical, biological and molecular features. Ann Intern Med 1985; 103:694-9.
29. Keshet E, Temin HM. Cell-killing by spleen necrosis virus is correlated with a transient accumulation of spleen necrosis virus DNA. J Virol 1979; 31:376-88.
30. Yarchoan R, Mitsuya H, Broder S. Immunologic issues in anti-retroviral therapy. Immunol Today 1990; 11:327-33.
31. Fischl MA, Richman DD, Grieco MH, et al The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex: a double-blind, placebo-controlled trial. N Engl J Med 1987; 317:185-91.
32. Volberding PA, Lagakos SW, Koch MA, et al Zidovudine in asymptomatic human immunodeficiency virus infection: a controlled trial in persons with fewer than 500 CD4-positive cells per cubic millimeter. N Engl J Med 1990; 322:941-9.
33. Sandstrom EG, Kaplan JC, Byington RE, Hirsch MS. Inhibition of human T-cell lymphotropic virus type III in vitro by phosphonoformate. Lancet

1985; 1:1480-2.
34. Schnittman SM, Psallidopoulos MC, Lane HC, et al The reservoir for HIV-1 in human peripheral blood is a T cell that maintains expression of CD4. Science 1989; 245:305-8.
35. Cullen BR, Greene WC. Regulatory pathways governing HIV-1 replication. Cell 1989; 58:423-6.
36. Rosenberg ZF, Fauci AS. Activation of latent HIV infection. J NIH Res 1990; 2:41-5.
37. Lenardo MJ, Baltimore D. NF-kappaB: a pleiotropic mediator of inducible and tissue-specific gene control. Cell 1989; 58:227-9.
38. Greene WC, Bohnlein E, Ballard DW. HIV-1, HTLV-1 and normal T cell growth: transcriptional strategies and surprises. Immunol Today 1989; 10:272-8.
39. Hoyos B, Ballard DW, Bohnlein E, Siekevitz M, Greene WC. Kappa B-specific DNA binding proteins: role in the regulation of the human interleukin-2 gene expression. Science 1989; 244:457-60.
40. Bohnlein E, Lowenthal JW, Siekevitz M, Ballard DW, Franza BR, Greene WC. The same inducible nuclear proteins regulates mitogen activation of both the interleukin-2 receptor-alpha gene and type 1 HIV. Cell 1988; 53:827-36.
41. Nabel G, Baltimore D. An inducible transcription factor activates expression of human immunodeficiency virus in T cells. Nature 1987; 326:711-3.
42. Jones KA, Kadonaga JT, Luciw PA, Tjian R. Activation of the AIDS retrovirus promoter by the cellular transcription factor, Spl. Science 1986; 232:755-9.
43. Zack JA, Arrigo SJ, Weitsman SR, Go AS, Haislip A, Chen IS. HIV-1 entry into quiescent primary lymphocytes: molecular analysis reveals a labile, latent viral structure. Cell 1990; 61:213-22.
44. Kim S, Byrn R, Groopman J, Baltimore D. Temporal aspects of DNA and RNA synthesis during human immunodeficiency virus infection: evidence for differential gene expression. J Virol 1989; 63:3708-13.
45. Dayton A, Sodroski JG, Rosen CA, Goh WC, Haseltine WA. The trans-activator gene of the human T cell lymphotropic virus type III is required for replication. Cell 1986; 44:941-7.
46. Fisher AG, Feinberg MB, Josephs SF, et al The trans-activator gene of HTLV-III is essential for virus replication. Nature 1986; 320:367-70.
47. Sodroski J, Patarca R, Rosen C, Wong-Staal F, Haseltine W. Location of the trans-activating region on the genome of human T-cell lymphotropic virus type III. Science 1985; 229:74-7.
48. Arya SK, Guo C, Josephs SF, Wong-Staal F. Trans-activator gene of human T-lymphotropic virus type III (HTLV-III). Science 1985; 229:69-73.
49. Sadaie MR, Benter T, Wong-Staal F. Site-directed mutagenesis of two trans-regulatory genes (tat-III, trs) of HIV-1. Science 1988; 239:910-3.
50. Frankel AD, Bredt DS, Pabo CO. Tat protein from human immunodeficiency virus forms a metal-linked dimer. Science 1988; 240:70-3.
51. Hauber J, Perkins A, Heimer EP, Cullen BR. Trans-activation of human immunodeficiency virus gene expression is mediated by nuclear events. Proc Natl Acad Sci U S A 1987; 84:6364-8.
52. Pavlakis GN, Felber BK. Regulation of expression of human immunodeficiency virus. New Biol 1990; 2:20-31.
53. Sharp PA, Marciniak RA. HIV TAR: an RNA-enhancer? Cell 1989; 59:229-30.
54. Dingwall C, Ernberg I, Gait MJ, et al Human immunodeficiency virus 1 tat protein binds trans-activation-responsive region (TAR) RNA in vitro. Proc Natl Acad Sci U S A 1989; 86:6925-9.
55. Gaynor R, Soultanakis E, Kuwabara M, Garcia J, Sigman DS. Specific binding of a HeLa cell nuclear protein to RNA sequences in the human immunodeficiency virus transactivating region. Proc Natl Acad Sci U S A

1989; 86:4858-62.
56. Gatignol A, Kumar A, Rabson A, Jeang K-T. Identification of cellular proteins that bind to the human immunodeficiency virus type 1 trans-activation-responsive TAR element RNA. Proc Natl Acad Sci U S A 1989; 86:7828-32.
57. Cullen BR. Trans-activation of human immunodeficiency virus occurs via a bimodal mechanism. Cell 1986; 46:973-82.
58. Laspia MF, Rice AP, Mathews MB. HIV-1 Tat protein increases transcriptional initiation and stabilizes elongation. Cell 1989; 59:283-92.
59. Berkhout B, Gatignol A, Rabson AB, Jeang K-T. TAR-independent activation of the HIV-1 LTR: evidence that tat requires specific regions of the promoter. Cell 1990; 62:757-67.
60. Kao S-Y, Calman AF, Luciw PA, Peterlin BM. Anti-termination of transcription within the long-terminal repeat of HIV-1 by tat gene product. Nature 1987; 330:489-93.
61. Greene WC. Regulation of HIV-1 gene expression. Annu Rev Immunol 1990; 8:453-75.
62. Guy B, Kieny MP, Riviers Y, et al HIV F/3′ orf encodes a phosphorylated GTP-binding protein resembling an oncogene product. Nature 1987; 330:266-9.
63. Luciw PA, Cheng-Mayer C, Levy JA. Mutational analysis of the human immunodeficiency virus: the orf-B region down-regulates virus replication. Proc Natl Acad Sci U S A 1987; 84:1434-8.
64. Terwilliger E, Sodroski JG, Rosen CA, Haseltine WA. Effects of mutations within the 3′ orf open reading frame region of human T-cell virus type III (HTLV-III/LAV) on replication and cytopathogenicity. J Virol 1986; 60:754-60.
65. Ahmad N, Venkatesan S. Nef protein of HIV-1 is a transcriptional repressor HIV-1 LTR. Science 1988; 241:1481-5.
66. Niederman TM, Thielan BJ, Ratner L. Human immunodeficiency virus type 1 negative factor is a transcriptional silencer. Proc Natl Acad Sci U S A 1989; 86:1128-32.
67. Kim SY, Ikeuchi K, Byrn R, Groopman J, Baltimore D. Lack of a negative influence on viral growth by the nef gene of human immunodeficiency virus type 1. Proc Natl Acad Sci U S A 1989; 86:9544-8.
68. Hammes SR, Dixon EP, Malim MH, Cullen BR, Greene WC. Nef protein of human immunodeficiency virus type 1: evidence against its role as a transcriptional silencer. Proc Natl Acad Sci U S A 1989; 86:9549-53.
69. Cohen EA, Dehni G, Sodroski JG, Haseltine WA. Human immunodeficiency virus vpr product is a virion-associated regulatory protein. J Virol 1990; 64:3097-9.
70. Sodroski J, Goh WC, Rosen C, Dayton A, Terwilliger E, Haseltine W. A second post-transcriptional trans-activator gene required for HTLV-III replication. Nature 1986; 321:412-7.
71. Feinberg MB, Jarrett RF, Adovini A, Gallo RC, Wong-Staal F. HTLV-III expression and production involve complex regulation at the levels of splicing and translation of viral RNA. Cell 1986; 46:807-17.
72. Cullen BR, Hauber J, Campbell K, Sodroski JG, Haseltine WA, Rosen CA. Subcellular localization of the human immunodeficiency virus trans-acting art gene product. J Virol 1988; 62:2489-501.
73. Malim MH, Hauber J, Fenrick R, Cullen BR. Immunodeficiency virus rev trans-activator modulates expression of the viral regulatory genes. Nature 1988; 335:181-3.
74. Malim MH, Hauber J, Le S-Y, Maizel JV, Cullen BR. The HIV-1 rev trans-activator acts through a structured target sequence to activate the nuclear export of unspliced viral mRNA. Nature 1989; 338:254-7.
75. Chang DD, Sharp PA. Regulation by HIV Rev depends upon recognition of splice sites. Cell 1989; 59:789-95.
76. Malim MH, Bohnlein S, Hauber J, Cullen BR. Functional dissection of the

HIV-1 Rev trans-activator -- derivation of a trans-dominant repressor of Rev function. Cell 1989; 58:205-14.
77. Dayton ET, Powell DM, Dayton AI. Functional analysis of CAR, the target sequence for the Rev protein of HIV-1. Science 1989; 246:1625-9.
78. Malim MH, Tiley LS, McCarn DF, Rusche JR, Hauber J, Cullen BR. HIV-1 structural gene expression requires binding of the Rev trans-activator to its RNA target sequence. Cell 1990; 60:675-83.
79. Heaphy S, Dingwall C, Ernberg I, et al HIV-1 regulator of virion expression (Rev) protein binds to an RNA stem-loop structure located within the Rev response element. Cell 1990; 60:685-93.
80. Zapp ML, Green MR. Sequence-specific RNA binding by the HIV-1 Rev protein. Nature 1989; 342:714-6.
81. Daly TJ, Cook KS, Gray GS, Maione TE, Rusche JR. Specific binding of HIV-1 recombinant Rev protein to the Rev-responsive element in vitro. Nature 1989; 342:816-9.
82. Baltimore D. Intracellular immunization. Nature 1988; 335:395-6.
83. Benko DM, Schwartz S, Pavlakis GN, Felber BK. A novel human immunodeficiency virus type 1 protein, tev, shares sequences with tat, env and rev proteins. J Virol 1990; 64:2505-18.
84. Salfeld J, Gottlinger HG, Sia RA, Park RE, Sodroski JG, Haseltine WA. A tripartite HIV-1 tat-env-rev fusion protein. EMBO J 1990; 9:965-70.
85. Bryant ML, Heuckeroth RO, Kimata JT, Ratner L, Gordon JI. Replication of human immunodeficiency virus 1 and Moloney murine leukemia virus is inhibited by different heteroatom-containing analogs of myristic acid. Proc Natl Acad Sci U S A 1989; 86:8655-9.
86. Trono D, Feinberg MB, Baltimore D. HIV-1 Gag mutants can dominantly interfere with the replication of the wild-type virus. Cell 1989; 59:113-20.
87. Jacks T, Power MD, Masiarz FR, Luciw PA, Barr PJ, Varmus HE. Characterization of ribosomal frameshifting in HIV-1 gag-pol expression. Nature 1987; 331:280-3.
88. Lowe DM, Aitken A, Bradley C, et al HIV-1 reverse transcriptase: crystallization and analysis of domain structure by limited proteolysis. Biochemistry 1988; 27:8884-9.
89. McKeever BM, Navia MA, Fitzgerald PM, et al Crystallization of the aspartylprotease from the human immunodeficiency virus, HIV-1. J Biol Chem 1989; 264:1919-21.
90. Wlodawer A, Miller M, Jaskolski M, et al Conserved folding in retroviral proteases: crystal structure of a synthetic HIV-1 protease. Science 1989; 245:616-21.
91. McQuade TJ, Tomasselli AG, Liu L, et al A synthetic HIV-1 protease inhibitor with antiviral activity arrests HIV-like particle maturation. Science 1990; 247:454-6.
92. Meek TD, Lamberd DM, Dryer EG, et al Inhibition of HIV-1 protease in infected T-lymphocytes by synthetic peptide analogues. Nature 1990; 343:90-2.
93. Klimkait T, Strebel K, Hoggan MD, Martin MA, Orenstein JM. The human immunodeficiency virus type 1-specific protein vpu is required for efficient virus maturation and release. J Virol 1990; 64:621-9.
94. Sodroski J, Goh WC, Rosen C, et al Replicative and cytopathic potential of HTLV-III/LAV with sor gene deletions. Science 1986; 231:1549-53.
95. Strebel K, Daugherty D, Clouse K, Cohen D, Folks T, Martin MA. The HIV 'A' (sor) gene product is essential for virus infectivity. Nature 1987; 328:728-30.
96. Lifson JD, Reyes GR, McGrath MS, Stein BS, Engelman EG. AIDS retrovirus induced cytopathy: giant cell formation and involvement of CD4 antigen. Science 1986; 232:1123-7.
97. Sodroski J, Goh WC, Rosen C, Campbell K, Haseltine W. Role of the HTLV-III/LAV envelope in syncytium formation and cytopathicity. Nature 1986; 322:470-4.

98. Leonard R, Zagury D, Desportes I, Bernard J, Zagury J-F, Gallo RC. Cytopathic effect of human immunodeficiency virus in T4 cells is linked to the last stage of virus infection. Proc Natl Acad Sci U S A 1988; 85:3570-4.
99. Levy JA, Kaminsky LS, Morrow WJW, et al Infection by the retrovirus associated with the acquired immunodeficiency syndrome: clinical, biological and molecular features. Ann Intern Med 1985; 103:694-9.
100. Gupta S, Vayuvegula B. Human immunodeficiency virus-associated changes in signal transduction. J Clin Immunol 1987; 7:486-9.
101. Lynn WS, Tweedale A, Cloyd MW. Human immunodeficiency virus (HIV-1) cytotoxicity: perturbation of the cell membrane and depression of phospholipid synthesis. Virology 1988; 163:43-51.
102. Rook AH, Lane HC, Folks T, McCoy S, Alter H, Fauci AS. Sera from HTLV-III/LAV antibody-positive individuals mediate antibody-dependent cellular cytotoxicity against HTLV-III/LAV-infected T cells. J Immunol 1987; 138:1064-7.
103. Lyerly HK, Matthews TJ, Langlois AJ, Bolognesi DP, Weinhold KJ. Human T-cell lymphotrophic virus type IIIB glycoprotein (gp120) bound to CD4 determinants on normal lymphocytes and expressed by infected cells serves as a target for immune attack. Proc Natl Acad Sci U S A 1987; 84:4601-5.
104. Walker BD, Chakrabarti S, Moss B, et al HIV-specific cytotoxic T lymphocytes in seropositive individuals. Nature 1987; 328:345-8.
105. Matthews TJ, Langlois AJ, Robey WG, et al Restricted neutralization of divergent human T-lymphotropic virus type III isolates by antibodies to the major envelope glycoprotein. Proc Natl Acad Sci U S A 1986; 83:9709-13.
106. Berman PW, Groopman JE, Gregory T, et al Human immunodeficiency virus type 1 challenge of chimpanzees immunized with recombinant envelope glycoprotein gp120. Proc Natl Acad Sci U S A 1988; 85:5200-4.
107. Arthur LO, Bess JW Jr, Waters DJ, et al Challenge of chimpanzees (Pan troglodytes) immunized with human immunodeficiency virus envelope glycoprotein gp120. J Virol 1989; 63:5046-53.
108. Gardner MB. Vaccination against SIV infection and disease. AIDS Res Hum Retroviruses 1990; 6:835-46.
109. Berman PW, Gregory TJ, Riddle L, et al Protection of chimpanzees from infection by HIV-1 after vaccination with recombinant glycoprotein gp120 but not gp160. Nature 1990; 345:622-5.

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Drug Therapy -- Clinical Pharmacology Of 3'-azido-2',3'-dideoxythymidine (zidovudine) And Related Dideoxynucleosides (Medical Intelligence)

Yarchoan, Robert; Mitsuya, Hiroaki; Myers, Charles E.; Broder, Samuel.
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following information: Charles Myers is an equity holder in Bristol Myers and has agreed to become a paid member of a drug monitoring committee for Adria Laboratories. Samuel Broder, Hiroaki Mitsuya, and Robert Yarchoan are coinventors on government patents for 2',3'-dideoxycytidine, 2',3'-dideoxyadenosine, and 2',3'-dideoxyinosine, as full-time employees of the U.S. government under the terms of the Federal Technology Transfer Act. All rights, title, and interest to these patents have been assigned to the government, which gives part of the royalties it receives to its employee inventors.

CITED REFERENCES

1. Gottlieb MS, Schroff R, Schanker HM, et al. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. N Engl J Med 1981; 305:1425-31.
2. Masur H, Michelis MA, Greene JB, et al. An outbreak of community-acquired Pneumocystis carinii pneumonia: initial manifestation of cellular immune dysfunction. N Engl J Med 1981; 305:1431-8.
3. Siegal FP, Lopez C, Hammer GS, et al. Severe acquired immunodeficiency in male homosexuals, manifested by chronic perianal ulcerative herpes simplex lesions. N Engl J Med 1981; 305:1439-44.
4. Barre-Sinoussi F, Chermann JC, Rey F, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 1983; 220:868-71.
5. Gallo RC, Salahuddin SZ, Popovic M, et al. Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. Science 1984; 224:500-3.
6. Popovic M, Sarngadharan MG, Read E, Gallo RC. Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. Science 1984; 224:497-500.
7. Mitsuya H, Popovic M, Yarchoan R, Matsushita S, Gallo RC, Broder S. Suramin protection of T cells in vitro against infectivity and cytopathic effect of HTLV-III. Science 1984; 226:172-4.
8. Mitsuya H, Weinhold KJ, Furman PA, et al. 3'-Azido-3'-deoxythymidine (BW A509U): an antiviral agent that inhibits the infectivity and cytopathic effect of human T-lymphotropic virus type III/lymphadenopathy-associated virus in vitro. Proc Natl Acad Sci USA 1985; 82:7096-100.
9. Ostertag W, Roesler G, Krieg CJ, et al. Induction of endogenous virus and of thymidine kinase by bromo-deoxy-uridine in cell cultures transformed by Friend virus. Proc Natl Acad Sci USA 1974; 71:4980-5.
10. de Clercq E. Suramin: a potent inhibitor of the reverse transcriptase of RNA tumor viruses. Cancer Lett 1979; 8:9-22.
11. Furmanski P, Bourguignon GJ, Bolles CS, Corombos JD, Das MR. Inhibition by 2',3'-dideoxythymidine of retroviral infection of mouse and human cells. Cancer Lett 1980; 8:307-15.
12. Waqar MA, Evans MJ, Manly KF, Hughes RG, Huberman JA. Effects of 2',3'-dideoxynucleosides on mammalian cells and viruses. J Cell Physiol 1984; 121:402-8.
13. Mitsuya H, Broder S. Inhibition of the in vitro infectivity and cytopathic effect of human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV) by 2',3'-dideoxynucleosides. Proc Natl Acad Sci USA 1986; 83:1911-5.
14. Mitsuya H, Matsukura M, Broder S. Rapid in vitro screening systems for assessing activity of agents against HTLV-III/LAV. In: Broder S, ed. AIDS: modern concepts and therapeutic challenges. New York: Marcel Dekker, 1987:303-33.
15. Balzarini J, Pauwels R, Herdewijn P, et al. Potent and selective

anti-HTLV-III/LAV activity of 2',3'-dideoxycytidinene, the 2',3'-unsaturated derivative of 2',3'-dideoxycytidine. Biochem Biophys Res Commun 1986; 140:735-42.
16. Hamamoto Y, Nakashima H, Matsui T, Matsuda A, Ueda T, Yamamoto N. Inhibitory effect of 2',3'-didehydro-2',3'-dideoxynucleosides on infectivity, cytopathic effects, and replication of human immunodeficiency virus. Antimicrob Agents Chemother 1987; 31:907-10.
17. Balzarini J, Kang G-J, Dalal M, et al. The anti-HTLV-III (anti-HIV) and cytotoxic activity of 2',3'-didehydro-2',3'-dideoxyribonucleosides: a comparison with their parenteral 2',3'-dideoxyribonucleosides. Mol Pharmacol 1987; 32:162-7.
18. Lin T-S, Schinazi RF, Prusoff WH. Potent and selective in vitro activity of 3'-deoxythymidin-2'ene (3'-deoxy-2',3'-didehydrothymidine) against human immunodeficiency virus. Biochem Pharmacol 1987; 36:2713-8.
19. Schinazi RF, Chu C-K, Ahn M-K, et al. Selective in vitro inhibition of human immunodeficiency virus (HIV) replication by 3'-azido-2',3'-dideoxyuridine (CS-87). J Clin Biochem 1987; Suppl 11D:74. abstract.
20. Kim C-H, Marquez VE, Broder S, Mitsuya H, Driscoll JS. Potential anti-AIDS drugs: 2',3'-dideoxycytidine analogues. J Med Chem 1987; 30:862-6.
21. Marquez VE, Tseng CK, Kelly JA, et al. 2',3'-Dideoxy-2'-fluoro-ara-A: an acid-stable purine nucleoside active against human immunodeficiency virus (HIV). Biochem Pharmacol 1987; 36:2719-22.
22. Herdewijn P, Balzarini J, De Clercq E, et al. 3'-Substituted 2',3'-dideoxynucleoside analogues as potential anti-HIV (HTLV-III/LAV) agents. J Med Chem 1987; 30:1270-8.
23. Balzarini J, Robins MJ, Zou RM, Herdewijn P, De Clercq E. The 2',3'-dideoxyriboside of 2,6-diaminopurine and its 2',3'-didehydro derivative inhibit the deamination of 2',3'-dideoxyadenosine, an inhibitor of human immunodeficiency virus (HIV) replication. Biochem Biophys Res Commun 1987; 145:277-83.
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US PAT NO: 5,292,636 [IMAGE AVAILABLE] L6: 1 of 5

ABSTRACT:
The present invention is directed to the measurement of soluble T cell growth factor receptors, soluble T cell differentiation antigens, or related soluble molecules or fragments thereof, and the use of such measurements in the diagnosis, staging, and therapy of diseases and disorders. Specific embodiments involve the diagnosis and monitoring of therapy using absolute values of such soluble molecules. Further embodiments involve detecting a change in the levels of such soluble molecules, in the diagnosis and therapy of diseases and disorders. In specific embodiments, measurements of interleukin-2 receptor levels can be made to detect lung cancer, or to stage squamous cell lung carcinoma. In other embodiments, detection of increases in both soluble IL2R and creatinine in the body fluid of a transplant patient can be used to differentially diagnose renal allograft rejection from infection. The invention is also directed to methods for measurement of soluble CD4 antigens, which measurements can be used, in a specific embodiment, to diagnose a state of immune activation, to diagnose rheumatoid arthritis, to monitor therapeutic efficacy (e.g. of AIDS treatments), or to stage adult T cell leukemia in a patient. In another aspect, the invention relates to the detection, staging, and monitoring of therapy of diseases and disorders by measuring a plurality of soluble T cell markers.

1. 5,292,636, Mar. 8, 1994, Therapeutic and diagnostic methods using soluble T cell surface molecules; Patrick C. Kung, et al., 435/5, 7.23, 7.24, 7.9, 7.94, 34, 974, 975; 436/506, 518, 536, 548, 811, 813 [IMAGE AVAILABLE]

US PAT NO: 5,262,177 [IMAGE AVAILABLE] L6: 2 of 5

ABSTRACT:
Peptides or proteins related to a melanoma associated antigen are described. These are produced in large quantities via recombinant DNA techniques and/or by chemical synthetic methods. The peptides or proteins can be used as immunogens in vaccine formulations which can induce an immune response that selectively destroys melanoma cells in a vaccinated individual. Where the peptides or proteins are expressed by a recombinant virus, inactivated or live virus vaccine formulations may be prepared.

2. 5,262,177, Nov. 16, 1993, Recombinant viruses encoding the human melanoma-associated antigen; Joseph P. Brown, et al., 435/235.1;

424/185.1, 199.1, 232.1; 435/69.3, 172.3, 240.2, 252.3, 252.33, 320.1; 530/350; 536/23.5; 935/9, 32, 41, 57, 65, 70, 73 [IMAGE AVAILABLE]

US PAT NO: 5,141,742 [IMAGE AVAILABLE] L6: 3 of 5

ABSTRACT:
Peptides or proteins related to a melanoma associated antigen are described. These are produced in large quantities via recombinant DNA techniques and/or by chemical synthetic methods. The peptides or proteins can be used as immunogens in vaccine formulations which can induce an immune response that selectively destroys melanoma cells in a vaccinated individual. Where the peptides or proteins are expressed by a recombinant virus, inactivated or live virus vaccine formulations may be prepared.

3. 5,141,742, Aug. 25, 1992, Vaccines against melanoma; Joseph P. Brown, et al., 424/186.1, 277.1; 435/69.3, 70.1, 71.1, 71.2; 530/350, 395; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,041,379 [IMAGE AVAILABLE] L6: 4 of 5

ABSTRACT:
The present invention relates to recombinant vector/host systems which can direct the expression of foreign genes under the control of the Heliothis polyhedrin promoter. Using the systems of the present invention, a heterologous gene of interest can be expressed as an unfused peptide or protein, a fusion protein, or as a recombinant occlusion body which comprises crystallized polyhedrin fusion proteins bearing the heterologous gene product on the surface of or within the occlusion body. The recombinant proteins or occlusion bodies of the present invention have uses in vaccine formulations and immunoassays, as biological insecticides, and as expression systems for the production of foreign peptides or proteins.

4. 5,041,379, Aug. 20, 1991, Heliothis expression systems; Malcolm J. Fraser, et al., 435/235.1, 69.1, 70.1, 172.3, 240.2, 320.1; 536/23.2, 23.6, 23.72; 935/3, 6, 9, 22, 33, 34, 47, 48, 59, 60, 61, 66, 70 [IMAGE AVAILABLE]

US PAT NO: 4,855,224 [IMAGE AVAILABLE] L6: 5 of 5

ABSTRACT:
A molecularly cloned diagnostic product in the form of a polypeptide with antigenic determinants capable of specifically binding complementary antibody, the polypeptide being expressed from a stable continuous cell line. With a glycoprotein D of Herpes Simplex Virus (HSV) as the polypeptide , HSV antibody in a specimen is detected in an immunological procedure. With a glycoprotein C fragment from HSV type 2, HSV type 2 may be distinguished from HSV type 1.

5. 4,855,224, Aug. 8, 1989, Molecularly cloned diagnostic product and method of use; Phillip W. Berman, et al., 435/5, 172.3, 240.2; 930/224 [IMAGE AVAILABLE]

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